REMARKS

Amendments

Claim 3 is incorporated in claim 1 and hence is cancelled as moot. The language from claim 6 concerning binding an Fc gamma receptor III (FcγRIII) with better affinity is also incorporated in claim 1. In addition, claim 1 is amended to refer to "two or more amino acid substitutions in the Fc region," with basis for this language found in claim 12, for example.

The 276, 309, 320, 322, 331, and 334 positions are deleted from claim 14. Applicants note for the record that claim 14 still encompasses Fc region modification(s) at position(s) 276, 309, 320, 322, 331, and/or 334 provided such modification(s) are combined with modification(s) at other position(s) recited in claim 14.

In view of the restriction requirement, the preamble for claim 14 is amended to refer to "a variant Fc region with increased binding to an Fc gamma receptor (FcγR)."

Claims 50-61 are added herein and find support at least as follows: claim 50 (claim 11); claim 51 (claim 12); claim 52 (claim 13); claim 53 (claim 2); claims 54-55 (claim 11); claims 56-58 (page 28, lines 15-17); claims 59-60 (claim 4); and claim 61 (claims 1, 4, 6 and 12).

In that the amendments do not introduce new matter, entry thereof is respectfully requested.

Section 112, 2nd paragraph

Claim 10 is rejected under 35 USC Section 112, second paragraph.

With respect to claim 10, the Examiner contends that the term "lower hinge region" therein is indefinite in that the specification provides no bound (*e.g.* residue position) for the term "lower hinge region." Applicants respectfully submit that the specification does provide the residue positions for the lower hinge region on page 16, lines 21-24. Since the claims should be read in light of the specification, Applicants submit that the term "lower hinge region" in claim 10 is clear. Reconsideration and withdrawal of the rejection is respectfully requested.

Restriction Requirement

The Examiner requests that claim 14 be amended to reflect the elected embodiment of claim 1. Applicants have followed the Examiner's request, amending claim 14, without prejudice or disclaimer to refer to "increased binding to an Fc gamma receptor (FcγR)" (see Restriction Requirement dated 9/25/01, Paper # 11, page 2, which refers to the invention of group I, namely, "engineered antibodies with increased ADCC activity or binding affinity for an FcγR").

Section 102 & 103 - Better *et al.*

Claims 1-2, 5-6 and 8-10 are rejected under 35 USC Section 102(b) as being anticipated, and claims 1 and 36-37 are rejected under 35 USC Section 103(a) as being unpatentable, over US Patent 5,576,184 (Better *et al.*).

These rejections are moot in view of the incorporation of claim 3, which is not rejected, into claim 1. Reconsideration and withdrawal of the Section 102 and 103 rejections based on Better *et al.* is respectfully requested.

Section 102(b) - Chappel *et al.*

Claims 1-4, 8-9, 14-15 and 36 are rejected under 35 USC Section 102(b) as being anticipated by Chappel *et al. JBC* 268:25124-25131 (1993). The Examiner urges that Chappel *et al.* show mutated forms of human IgG1 and IgG2 antibodies which show increased binding to FcγRI.

With respect to claim 1, the rejection is moot in view of the incorporation of the language of claim 6, which is not rejected, into claim 1. As to claim 14, the rejection is moot in view of the deletion of position 309 from that claim. Reconsideration and withdrawal of the rejection over Chappel *et al.* is respectfully requested.

Section 102(b) - Sarmay *et al.*

Claims 1-5 and 8-9 are rejected under 35 USC Section 102(b) as being anticipated by Sarmay *et al. Molec. Immunol.* 29:633 (1992). The Examiner contends that Sarmay *et al.* teach a mouse-human IgG2b chimeric antibody mutated at position 235, from Glu to Leu and that this mutation provides an antibody having increased ADCC activity.

First, Applicants note that the IgG2b antibody is actually a mouse antibody with a point mutation at position 235 in the mouse Fc region (see the abstract for instance), rather than in a human IgG Fc region, and hence the rejection is moot in view of the incorporation of claim 3 in claim 1. Moreover, Sarmay *et al.* fails to disclose or suggest a variant comprising two or more amino acid substitutions in the Fc region as in claim 1 herein. Reconsideration and withdrawal of the rejection over Sarmay *et al.* is respectfully requested.

Section 102(b) - Morgan *et al.*

Claims 1-4, 8-10, 14-15, 23, 27-28 and 36 are rejected under 35 USC Section 102(b) as being anticipated by WO94/29351 (Morgan *et al.*) The Examiner urges that Morgan *et al.* discloses (pp. 16-17) a human IgG1 antibody having a K320A mutation, which inherently has all the features of claims 1-4, 8-10, 14-15, 23 and 27-28.

As to claim 1, the rejection is moot in view of the incorporation of the language from claim 6, which is not rejected, into claim 1. Turning now to independent claim 14 herein, position 320 is deleted from the claim, thus obviating the rejection insofar as it applies to claim 14. Reconsideration and withdrawal of the rejection over Morgan *et al.* is respectfully requested.

Section 102(e) - Idusogie *et al.*

Claims 1-6, 8-11, 14-15, 23-24, 26-30 and 36-37 are rejected under 35 USC Section 102(e) as being anticipated by US Patent No. 6,242,195 (Idusogie *et al.*). The Examiner states that Idusogie *et al.* discloses the existence of mutant forms N276A, K320A, K322A, P331A, K334 which were assessed for their ability to bind C1q and activate complement.

With respect to claim 1, the rejection is moot in view of the recitation in claim 1 that the variant comprises "two or more amino acid substitutions" in the Fc region, which language can be found in claim 12, which claim was not rejected over Idusogie *et al.* With respect to independent claim 14 herein, positions 276, 320, 322, 331, and 334 are deleted from the claim, thus obviating the rejection insofar as it applies to claim 14. Reconsideration and withdrawal of the rejection over Idusogie *et al.* is respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1 and 14 have been amended as follows.

1. (Amended) A variant of a parent polypeptide comprising [an] a human IgG Fc region, which variant mediates antibody-dependent cell-mediated cytotoxicity (ADCC) in the presence of human effector cells more effectively, or binds an Fc gamma receptor III (FcγRIII) with better affinity, than the parent polypeptide and comprises [at least one amino acid modification] two or more amino acid substitutions in the Fc region.

14. (Amended) A polypeptide comprising a variant Fc region with [altered] increased binding to an Fc gamma receptor (FcγR) [binding affinity], which polypeptide comprises an amino acid modification at any one or more of amino acid positions 238, 239, 248, 249, 252, 254, 255, 256, 258, 265, 267, 268, 269, 270, 272, [276,] 278, 280, 283, 285, 286, 289, 290, 292, 293, 294, 295, 296, 298, 301, 303, 305, 307, [309,] 312, 315, [320, 322,] 324, 326, 327, 329, 330, [331,] 333, [334,] 335, 337, 338, 340, 360, 373, 376, 378, 382, 388, 389, 398, 414, 416, 419, 430, 434, 435, 437, 438 or 439 of the Fc region, wherein the numbering of the residues in the Fc region is that of the EU index as in Kabat.

Claim 3 has been cancelled without prejudice or disclaimer.

Claims 50-61 have been added.